Pediatric Gastrointestinal Motility Disorders: Challenges and a Clinical Update

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Abstract: Pediatric gastrointestinal motility disorders are common and can range from relatively benign conditions such as functional constipation to more serious disorders such as achalasia, Hirschsprung disease, and intestinal pseudoobstruction. Performing and interpreting motility evaluations in children presents unique challenges and is complicated by a dearth of control information, underlying gastrointestinal developmental maturation, technical challenges (eg, catheter size limitations), and patient cooperation. Primary diseases such as congenital pseudoobstruction or Hirschsprung disease occur more often in children, but as with adults, abnormal motility may be secondary to other processes. Diagnostic studies include radiographic studies, manometry, breath testing, myoelectrical testing, and histologic evaluation. Although recent advances in technology, genetics, and biology are making an important impact and have allowed for a better understanding of the pathophysiology and therapy of gastrointestinal motility disorders in children, further research and new therapeutic agents are needed.

Keywords
Pediatric motility disorders, Hirschsprung disease, intestinal pseudoobstruction, achalasia

Pediatric gastrointestinal motility disorders are common and can range from often benign conditions such as chronic constipation to more serious primary motility disorders such as esophageal achalasia, Hirschsprung disease (HD), or chronic intestinal pseudoobstruction (CIPO).[1]

Although motility disorders in children share many characteristics with those seen in adults, there are often important differences in the diagnosis and management between the two groups. Performing evaluations for motility disorders in pediatric patients has unique and challenging considerations. This review provides a brief overview of the challenges encountered in performing motility evaluations in children and focuses on aspects of diagnosis and therapy of primary motor disorders that are unique to pediatric patients.

Evaluation of the Pediatric Patient With a Suspected Motility Disorder

When the symptoms of a child are suggestive of a gastrointestinal motility disorder, careful evaluation for anatomic, mucosal, or metabolic disorders should be undertaken (Table 1).[2-5] Excluding an anatomic cause via radiographic or endoscopic studies is the most important first step after obtaining a thorough history and conducting a physical examination. If an anatomic problem is not present, examinations of various aspects of gastrointestinal motor function may be conducted while other processes are also being evaluated.[5]

The manometric evaluations most commonly performed in the pediatric population include those of esophageal and anorectal origin, though colonic and antroduodenal testing are also being performed with increasing frequency.[4-6] The primary indications for the various manometric studies in children are listed in Table 2.

Challenges Unique to the Pediatric Population

Performing motility evaluations in the pediatric population offers unique challenges. The first challenge is related to the development and maturation of the gastrointestinal system. After birth, motor processes begin to mature until they develop adult characteristics. These processes, ranging from enteric nervous system maturation to contractile patterns, are still being elucidated[7-11] and are beyond the scope of this review.

The second challenge is the difficulty of interpreting evaluations given the sparse child-control data. The majority of "normal" values have been derived by applying data from adults or by reviewing data obtained in children categorized as normal a posteriori. This practice has been seen particularly in more invasive studies such as antroduodenal or colonic manometries and in age groups outside neonates and late adolescents. The lack of child-specific information can make analysis more difficult, and care must be taken to avoid overinterpretation,[4,5,12] as certain patterns deemed to be abnormal in adults may in fact be normal in children.

The third challenge involves technical aspects unique to the performance of manometry and other evaluations in the pediatric population.[12] These aspects include limitations with regard to the available equipment such as catheter size, the amount and type of fluid used in perfusion systems, and the lack of cooperation that may be found, particularly in the youngest children. Of particular concern in the performance of prolonged studies in young children is the administration of large amounts of fluid with the usage of perfused manometry. Given the risk of water intoxication during prolonged studies, the majority of pediatric laboratories use sodium-containing solutions. Recently, silicon extrusion tubing has allowed for the creation of smaller catheters with sleeves.[9,13,14] These advances have permitted the study of premature infants and have provided information on developmental

Table 1. Approach to the Pediatric Patient With a Suspected Motility Disorder

1. **Exclude anatomic problems (the most important initial step, which should be undertaken in all patients).**
   - Radiography: plain films, upper gastrointestinal series with small-bowel follow-through, barium enema
   - Endoscopy
2. **Exclude mucosal or metabolic disorders.**
   - Endoscopy and biopsy, laboratory examinations (eg, metabolic, endocrine)
3. **Evaluate transit.**
   - pH probe/impedance
   - Scintigraphy
     - Gastric emptying
     - Esophageal emptying
     - Gallbladder emptying
     - Small bowel–colon transit
   - Barium
     - Videofluoroscopy barium swallow
     - Esophageal emptying
   - Other studies
     - Marker-perfusion studies
     - Oroanal transit: color markers, radiopaque markers
     - Orocecal transit: lactulose breath test
     - Colonic transit: radiopaque markers
     - Ultrasonography
     - Breath tests
     - Telemetry capsule with pH/pressure
4. **Evaluate contractile activity (which allows for differentiation of neuropathy or myopathy).**
   - Gastrointestinal manometry
5. **Evaluate myoelectrical activity.**
   - Electrogastrography, electromyography
6. **Establish etiology and other associated problems.**
   - Differentiate between primary and secondary motility disorder.
   - Exclude systemic illness (endocrine, connective tissue and neuromuscular diseases, metabolic illnesses [eg, mitochondrial], psychiatric problems, or other systemic illnesses).
   - Establish associated abnormalities (eg, malnutrition, metabolic imbalance, autonomic dysfunction, muscle/nerve abnormalities).

Adapted from Nurko SS. Gastrointestinal manometry: methodology and indications. In: Walker WA, et al, eds. *Pediatric Gastrointestinal Disease.* 4th ed. Philadelphia, Pennsylvania: BC Decker Inc.; 2004:1786-1808.

Table 2. Indications for Manometric Studies in Children

Esophageal Manometry
- To explain esophageal dysfunction that is not explained by anatomic or well-defined etiologies
- In the presence of dysphagia and odynophagia
- In the diagnosis of achalasia or other primary esophageal motor disorders
- To support the diagnosis of connective tissue diseases or other systemic illnesses
- In the posttreatment evaluation of patients with achalasia and recurrent symptoms
- In the presence of noncardiac chest pain
- In the presence of gastroesophageal reflux in which the diagnosis is not clear (to exclude primary motility disorders)
- Prior to fundoplication when a severe motility disorder is suspected
- To localize the lower esophageal sphincter before pH probe placement in patients with abnormal anatomy (eg, hiatal hernia)
- To study esophageal transit with the additional use of impedance

Anorectal Manometry
- To diagnose a nonrelaxing internal anal sphincter
- To diagnose pelvic floor dyssynergia
- To evaluate postoperative patients with Hirschsprung disease who have obstructive symptoms and to evaluate the effect of anal sphincter–directed therapies
- To evaluate patients with fecal incontinence
- To evaluate postoperative patients after imperforate anus repair
- To decide whether the patient is a candidate for biofeedback therapy

Antroduodenal Manometry
- To establish the presence of pseudoobstruction
- To classify pseudoobstruction into myopathic or neuropathic forms
- To exclude a motility problem as a basis of the patient's symptoms in children with normal findings but "apparent intestinal failure"
- To evaluate unexplained nausea and vomiting
- To distinguish between rumination and vomiting
- To exclude generalized motility dysfunction in patients with dysmotility elsewhere (eg, before colectomy)
- To evaluate patients with pseudoobstruction being considered for intestinal transplant
- To possibly help predict outcome after feeding or after drug use in patients with pseudoobstruction
- To possibly suggest unexpected obstruction

Colonic Manometry
- To evaluate selected patients with intractable constipation (ie, differentiate functional constipation from colonic pseudoobstruction)
- To evaluate children with pseudoobstruction for the establishment of the presence of colonic involvement and to characterize the relationship between motor activity and persistent symptoms
- To establish the pathophysiology of persistent symptoms in selected children with Hirschsprung disease, imperforate anus, intractable constipation, and other colorectal problems
- To assess colonic motor activity prior to intestinal transplant

Adapted from Di Lorenzo C, et al.[3]

processes.[7,9] In the case of solid-state catheters, transducer size and cost often present a limiting step to the reduction of catheter diameter.[9,13,14]

The final challenge involves the varying levels of cognition and cooperation in children, which add to the difficulty of performing motility evaluations.[4,5] Age-appropriate and developmentally appropriate techniques should be utilized to decrease patient anxiety, as anxiety may influence the observed motility patterns. Results may be difficult to interpret during crying or with movement artifacts. Those who perform studies in children should be familiar not only with the interpretation of these studies but also with the basic aspects of cognitive infant and childhood development. In pediatrics, studies are often performed by physicians or nurses, not by technicians. It is not uncommon to find children who refuse to cooperate with certain parts of the study (eg, swallowing on command) or who are unable to follow or understand what is asked of them (eg, anal squeeze). It is also important to allow parents to be present to allow for a greater level of cooperation, as well as to observe parent-child interactions.

On certain occasions, particularly in young children, sedation may be necessary to perform anorectal or esophageal manometry. Midazolam[15] and chloral hydrate[16] do not appear to affect gastrointestinal motility. For antroduodenal or colonic manometric evaluations, catheter placement is often performed under general anesthesia, with the initiation of the study the next day or after the effect of the general anesthesia has worn off.

Specific Motility Disorders in Children

It is beyond the scope of this review to describe every motility disorder that affects children. We focus only on those disorders that offer a unique perspective or represent important problems in children.

Esophageal Motor Disorders

Esophageal motor disorders are listed in Table 3.[4,17]

Table 3. Esophageal Motor Disorders in Children

Striated Muscle Predominant Disorders
- Oropharyngeal problems
- Cricopharyngeal dysfunction
- Abnormalities of resting tone
- Abnormalities in relaxation
- Neuromuscular disorders
- Neurologic disorders
- Muscular disorders
- Neuromuscular disorders
- Structural lesions
- Central nervous system malformations

Smooth Muscle Predominant Disorders

Primary esophageal motor disorders
- Achalasia
- Diffuse esophageal spasm
- Ineffective peristalsis
- Nutcracker esophagus

Secondary esophageal motor disorders
- Gastrointestinal disorders (eg, esophageal atresia)
- Congenital malformations
- Eosinophilic esophagitis
- Collagen vascular disease
- Neuromuscular disorders
- Graft-versus-host disease
- Infectious diseases
- Exogenous factors (eg, medications, caustic ingestions)
- Iatrogenic disorders
- Other

Adapted from Nurko SS.[17]

Proximal Esophageal Disorders Oropharyngeal dysphagia is characterized by the inability to transfer food or liquids in a successful manner from the mouth to the esophagus, as well as a failure to swallow or suck. Infants with prematurity, anatomic abnormalities including cleft palate or laryngeal cleft, genetic disorders such as Riley Day syndrome, velocardiofacial syndrome, or other neurologic disorders may be affected.[18,19] Signs and symptoms in children include excessive salivation, nasal reflux, choking, cough, and cyanosis associated with alimentation. Aspiration may also occur, and swallowing problems may present with silent aspiration or aspiration pneumonia.[20] Congenital cricopharyngeal achalasia is a rare primary motility disorder of unknown etiology in which the upper esophageal sphincter fails to relax normally during swallowing due to cricopharyngeal muscle dysfunction, and the disorder presents with many of the above symptoms during infancy.[19] When cricopharyngeal dysfunction is suspected, cineradiographic or barium evaluation should be undertaken to examine swallowing and exclude anatomic abnormalities.[4,20] The classic finding of a posterior pharyngeal bar points toward cricopharyngeal dysfunction, though up to 5% of normal individuals may have this finding.[19] Esophageal manometry is useful in determining the function of the upper esophageal sphincter and for diagnosing cricopharyngeal achalasia.[4,20,21]

Treatment for oropharyngeal dysphagia may be specific (eg, correction of anatomic abnormalities) or nonspecific (eg, nutritional support and treatment of infections due to aspiration).[17,21] The dysphagia associated with systemic or neurologic disorders may improve with treatment of these disorders or with rehabilitation, depending upon the overarching diagnosis. In order to prevent laryngeal penetration, postural changes and/or dietary modifications such as avoiding liquids or increasing viscosity are often undertaken. Nutritional support with the placement of nasogastric tubes and/or gastrostomies may also be required.

Cricopharyngeal achalasia therapy in children has primarily been reported in case series and classically involves myotomy[19] or cricopharyngeal balloon dilatation.[18] Case reports of transient *Clostridium botulinum* toxin efficacy are emerging.[22] Spontaneous resolution has been reported to occur in neonates, potentially due to developmental maturation.[22]

Motor Disorders of Esophageal Smooth Muscle: Achalasia Esophageal achalasia is a primary esophageal motor disorder that presents with obstructive symptoms at the gastroesophageal junction. Achalasia is uncommon, with a prevalence of 1 in 100,000 people.[23] It is estimated that less than 5% of patients with achalasia develop symptoms before 15 years of age.[23] The median age for diagnosis in children is approximately 8 years,[17] and infant cases have been reported.[24]

The presentation of achalasia varies according to age.[17] In a recent review of 475 pediatric achalasia cases, 80% presented with vomiting, 76% with dysphagia, 61% with weight loss, 44% with respiratory symptoms, 38% with thoracic pain, 31% with growth failure, and 21% with nocturnal regurgitation.[17] In general, the youngest children have more respiratory symptoms. The dysphagia is often gradual and progressive, initially

involving solids and progressing toward intermittent liquid involvement. Regurgitation and vomiting is of undigested food.

The diagnosis of achalasia requires esophageal manometry. As with adults, achalasia is characterized by the following manometric abnormalities: lack of esophageal peristalsis; increased lower esophageal sphincter pressure; and partial or incomplete relaxation of the sphincter.[25-29] The only required finding is lack of peristalsis.[17,26-29]

The therapy of choice in children is controversial, particularly when one takes into account the lack of available long-term data. Treatment is focused on reducing pressure at the gastroesophageal junction, and pediatric experience using pharmacotherapy,[17,30] *C. botulinum* toxin injection,[31,32] pneumatic balloon dilatation,[17] and esophagomyotomy[33-36] is growing. Currently, the most effective treatments include pneumatic dilatation and esophagomyotomy.[17,35] In a literature review of 151 children with achalasia treated with pneumatic dilatation, excellent or good results were seen in 57%.[20] Other findings included perforation in 5.7% of the patients, severe reflux in 2%, dysphagia in 20%, and subsequent need for surgery in 25%. In 455 children undergoing traditional surgical esophagomyotomies, excellent or good results were seen in 77% of the patients, as well as postoperative reflux in 4%, dysphagia in 5%, need for re-operation in 5%, and death in 0.7%.[17]

More recently, minimally invasive surgery has been emerging as a popular therapeutic modality. Initial results from laparoscopic esophagomyotomies in children, the majority of which were coupled with fundoplication, were very promising, with very high initial success rates.[33,35] In one study, esophageal perforation occurred in 8.3% of the patients, dysphagia in 16.6%, and the need for repeat surgery in 8.3%.[33] Presently, the preferred treatment depends on the expertise available at the center. Future prospective evaluations with long-term follow-up surveillance of children with achalasia undergoing different therapeutic procedures may help determine which method is ideal.

Gastric Motor Disorders: Gastroparesis

Gastroparesis, or delayed gastric emptying without obstruction, occurs in children, but its incidence and prevalence has not been recently evaluated. The clinical symptoms consist principally of vomiting and epigastric discomfort. Concurrent nausea, bloating, and other dyspeptic symptoms may also be associated. As with adults, vomiting classically occurs late in the day postprandially and commonly contains foods eaten many hours beforehand. The prevalence and etiologies of gastroparesis in children has not been extensively examined, though postviral gastroparesis is thought to be the most common identifiable etiology in children. Postviral gastroparesis is often suggested by a history of fevers, myalgias, nausea, or diarrhea and may be confirmed in the laboratory.[37,38] All 11 children followed in one study with postviral gastroparesis went on to experience resolution of their symptoms within 2 years.[38] Idiopathic gastroparesis occurs in the absence of a systemic disease or other identifiable etiology, and it is often how children without postviral gastroparesis are eventually categorized.[39,40] Other etiologies in children include diabetes mellitus,[41] vagotomy, medications (eg, chemotherapeutic agents, anticholinergics), endocrinologic abnormalities (eg, hypothyroidism), foregut developmental abnormalities (eg, gastroschisis), neurologic disorders, and genetic/metabolic disorders[42] such as Riley Day syndrome.

The diagnosis in children is often made through nuclear medicine scintigraphy, though standardization of this evaluation in children is lacking, and varying emptying rates in normal children have been described.[43] Octanoic acid breath testing has been used and shown to be valid in children[44] and does not involve any radiation; however, it is not widely available. Antroduodenal manometry may demonstrate antral contractile abnormalities, particularly hypomotility.[2-5] Although this examination is thought to be sensitive and specific, it is more invasive. Electrogastrography has detected abnormalities that have been shown to correlate with gastroparesis,[45] but its clinical use in children is not well validated. The role that wireless telemetry pressure/pH capsules will have in the measurement of gastric emptying in children must be established in the future, though it will probably represent a useful technique in older children.

Initial therapy includes addressing any secondary etiologies, discontinuing medications known to slow gastric emptying, modifying the diet of the child to decrease gastric distention, and using appropriate nutritional support. Given that liquids empty more quickly than solids, avoiding high-residual indigestible solid food is desirable. Nasojejunal or surgical jejunostomies may be needed in order to provide enteral nutrition.

Pharmacotherapy may include conventional antiemetics to decrease nausea and vomiting. Prokinetic drugs designed to improve gastric emptying have improved treatment for gastroparesis in children,[2,46-48] though the evidence is sparse. These drugs include erythromycin, metoclopramide, domperidone, cisapride (Propulsid, Janssen), and tegaserod (Zelnorm, Novartis). Unfortunately there are major limitations for the pediatric use of the latter three medications. Baclofen has been shown to improve gastric emptying in one pediatric study.[45] *C. botulinum* pyloric injections have been used in children, but studies of its effectiveness in this population have not been published. Gastric electrical stimulation

studies have involved small numbers of children up to this point, and further evaluation is needed, though preliminary studies show promise.

Small Intestinal and Colonic Motor Disorders

The primary motor disorders that affect the small intestine and colon in children include conditions such as HD and CIPO, in which the motility disorder is directly responsible for the clinical presentation. In other conditions, such as irritable bowel syndrome and functional constipation, the motor problem is one of many factors that contribute to the presenting symptoms. These conditions are not discussed here.

Chronic Intestinal Pseudoobstruction CIPO is a rare disorder, and it is estimated that approximately 100 infants with congenital CIPO are born in the United States every year.[49] CIPO was defined by the Task Force of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition as "a severe disabling disease characterized by repetitive episodes or continuous symptoms and signs of intestinal obstruction, including radiographic documentation of dilated intestines and air-fluid levels, in the absence of fixed lesion which is occluding the lumen of the intestine."[50] The motor alterations lead to the inability for normal transit of nourishment and secretions along the gastrointestinal tract. Pediatric symptoms in one review included abdominal distention (98%), vomiting (91%), constipation (77%), failure to thrive (62%), abdominal pain (58%), sepsis (34%), and diarrhea (31%).[51] Any segment of the intestinal tract may be affected, and symptoms represent this heterogeneity. Intestinal dilation and slow transit predispose the patient to bacterial overgrowth, which may lead to malabsorption, diarrhea, and malnutrition.[50] In one review of 105 pediatric CIPO cases, approximately 75% presented within the first year of life, with 67% presenting within the first month.[51]

CIPO may be primary or secondary to different processes, and it may be part of syndromes such as megacystis, microcolon, or intestinal hypoperistalsis syndrome.[50] The majority of infantile forms are primary and spontaneous, with a small minority being hereditary familial processes. CIPO can also be secondary to mitochondrial disorders, diminished interstitial cells of Cajal, inflammatory conditions, or autoimmune disorders.[49] Primary and secondary forms are often classified into primarily myopathic or neuropathic processes. Associated intestinal abnormalities such as malrotation, gastroschisis, and atresias are seen in over 25% of pediatric CIPO cases.[52] Urinary abnormalities such as megacystis or urinary tract infections are found in a majority of congenital myopathic processes and in a minority of neuropathic processes.[53]

Diagnosis is initially determined clinically, and radiographic studies are utilized to exclude mechanical obstruction. Many children have more than one laparotomy before pseudoobstruction is formally diagnosed. Unfortunately, abdominal surgeries make it challenging to differentiate pseudoobstructive crises from obstruction caused by adhesions. An evaluation focused on the identification of potentially reversible secondary causes (eg, hypothyroidism) should be undertaken in all cases.

Antroduodenal and colonic manometry have been used to characterize intestinal involvement in children with CIPO, and they may also predict successful enteral nutrition support.[54-55] When myopathy is present, low-amplitude but normally organized contractions are found. With advanced disease, there is an absence of contractions. In neuropathy, contractions are of normal amplitude but are poorly organized, with groups of non-peristaltic contractions, prolonged tonic contractions, and persistence of a fasting motor pattern despite alimentation. Lack of normal migrating motor complexes suggests a neuropathic etiology. Care must be taken in interpreting manometric studies when severe intestinal dilation is present.[8]

CIPO is a disease with a high mortality and morbidity. In a study that followed 85 children with CIPO for a median of 25 months, 22 children perished.[56] Quality-of-life outcomes in children with CIPO and their families are significantly diminished.[56] Morbidity and mortality are related to the severity of intestinal abnormalities, with severe cases requiring parenteral nutrition. Although parenteral nutrition has saved the lives of children who cannot be given sufficient enteral nutrition, it is associated with the complications of sepsis, thromboembolic events, and liver disease with progressive failure. These complications lead to the majority of deaths seen in children with CIPO.[53]

A specific therapy is often not available, and supportive measures are used. Special attention must be placed on nutritional support. When possible, it is recommended that enteral nutrition be given. Low-fat liquid diets are emptied by the stomach more easily. Metabolic disorders, inflammatory processes, electrolyte abnormalities, and endocrinologic disorders that may contribute to the pathogenesis should be excluded. Medications that decrease gastrointestinal motility should not be used, and bacterial overgrowth should be treated aggressively. Surgical decompression through gastrostomies and ileostomies are frequently necessary. Prokinetics have occasionally been effective.[57]

Treatment of pain is important. Opioids worsen gastrointestinal motility and cause dependence. Tricyclic antidepressants, selective serotonin reuptake inhibitors, clonidine, gabapentin (Neurontin, Pfizer), and short peri-

ods of epidural anesthesia may be beneficial.[57] Successful bilateral thorascopic splanchnicectomy has been reported in 2 children.[58] Psychiatric support for the patient and family is helpful and provides important benefits.

Finally, small-bowel transplantation may provide the only hope for cure in patients with the most severe disease. Although more recently performed transplant results are likely to have improved outcomes, one report published in 2005 examining 12 small-bowel transplants in children with gastrointestinal dysmotility found a survival rate of 66.7% at 1 year and 50% at 3 years.[59]

Hirschsprung Disease Defecation problems in children are very common.[60-63] After the neonatal period, the most frequent cause of constipation in childhood is functional constipation. Discrete abnormalities in colonic motility are rarely an important pathogenic factor in these children. However, there are rare cases of constipation caused by primary motor abnormalities, which should not be missed.

The most common of these abnormalities is HD, which has an incidence varying from 1 in 5,000 to 1 in 10,000 live births.[1] HD is a congenital disease with varying degrees of aganglionosis, starting distally from the internal anal sphincter and moving proximally. The aganglionic segment is in a constant contractile state whereas proximal segments of intestine become dilated due to the distal functional obstruction.[64] The length of the aganglionic segment varies, as it is limited to the rectum and sigmoid in 75% of patients, affects the entire colon in 7% of patients, and rarely extends into the small intestine. The median age at the time of diagnosis has been decreasing over time; HD is established in 15% of patients in the first month, in 40–50% of patients in the first 3 months, in 60% of patients at the end of the first year, and in 85% of patients by 4 years of age.[63,64] Recent advances have shown that in some cases, identifiable genetic mutations (eg, proto-oncogene *RET* mutations) are associated with HD.[65]

Symptoms vary with age and the length of aganglionosis. In the newborn, HD may present with acute obstruction, bilious emesis, abdominal distention, and lack of meconium passage. If the diagnosis is not made, the infant will present with constipation, which may later be followed by abdominal obstruction, frequent episodes of impaction, or the development of enterocolitis. Enterocolitis may be involved in 15–50% of cases and may be the first sign of presentation in 12% of cases.[63] Enterocolitis continues to be the principal cause of death, with a mortality rate that can reach up to 20–50%.[63] From infancy through adulthood, constipation, which should be differentiated from functional constipation, may be the only symptom. Using clinical characteristics alone does not always distinguish the two, and therefore HD should be considered in all patients with intractable constipation.[50,61]

The diagnosis of HD is established through biopsy, which reveals a lack of ganglion cells. The usage of specialized stains such as the acetylcholinesterase stain aids in the diagnosis.[66,67] Given that obtaining biopsies carries risks, other less invasive techniques such as barium enema and anorectal manometry (ARM) may aide in excluding HD. ARM is clearly superior to barium enema for the diagnosis of HD.[68] However, in all cases, the diagnosis should be confirmed via biopsy.

Definitive therapy is surgical, though initial medical management is important to stabilize the patient and includes correction of electrolyte abnormalities and rectal decompression. In cases of enterocolitis, antibiotics should also be administered.[63] Surgery is aimed at resecting the aganglionic segment, followed by a pull-through of ganglionic segments to the rectum. The most frequently performed operations include the Swenson, Duhamel, and Soave. Recent advances have allowed for the use of laparoscopic or transrectal techniques in the newborn.[69] The complications and long-term outcomes associated with the different surgeries are similar.[63,70,71] Obstructive symptoms occur in a significant number of patients, and the treatment of these symptoms has included application of *C. botulinum* toxin directly to the sphincter,[72,73] myectomy,[74] and topical organic nitrate application.[75,76] Appendicectomies or cecostomies to apply antegrade continence enemas may be utilized in selected postsurgical HD patients with continued symptoms, as long as adequate treatments for the nonrelaxing sphincter are also instituted.[77] Colonic resection are rarely needed but may be necessary at times if severe localized motility abnormalities can be demonstrated.[63,70,71]

Other Colonic Neuromuscular Diseases Internal anal sphincter achalasia, formerly termed ultrashort HD, an entity in which rectal biopsies show ganglion cells but anorectal manometry demonstrates a lack of internal anal sphincter relaxation, has been described. Children with this condition may have significant constipation and abdominal distention due to the lack of sphincter relaxation. Therapy includes *C. botulinum* toxin injection[78] and posterior myectomy.[79]

In some children, severe constipation is related to neurenteric abnormalities of the colon. A lack of interstitial cells of Cajal and other neurotransmitter abnormalities have been described.[80] The motility abnormality can be demonstrated by colonic manometry, in which there are either generalized or segmental abnormalities.

Treatment is supportive. Laxatives and therapies directed at decreasing anal sphincter pressure are utilized. Rarely, surgical resections are required, but they can be targeted to the findings of the colonic manometry.

Appendicectomies or cecostomies are also used to provide antegrade enemas.[81] This operation allows for access to the proximal colon through the creation of a conduit to the skin. The procedure may be done surgically, with interventional radiology, or with endoscopy.[81-83] The results have been positive, particularly in patients with fecal incontinence due to neurologic problems and in patients with constipation.[81-83]

Future Advances

Genetic advances have allowed for the detection of the genes responsible for intestinal development and function. As previously mentioned, mutations that lead to HD have been found and are being extensively studied. The genetic basis of other intestinal motor disorders will likely be elucidated, and greater insight into the pathophysiology of these disorders will continue to emerge.

The utilization of new microperfusion systems and microcatheters will allow for the study of motility processes in smaller patients.[9] Moreover, newer techniques such as high-resolution manometry or telemetry studies will continue to be developed and add new perspectives in the understanding of motility disorders. Continued research of noninvasive diagnostic modalities such as electrogastrography may lead to less discomfort while maintaining a high degree of sensitivity and specificity for the diagnosis of these disorders. The usage of barostat is an experimental technique that has allowed for better study of the sensory aspects and new understanding of the relationship between wall tension, pressure/volume changes, and function. Its usage within pediatrics has been increasing and will allow for improved understanding of the pathophysiology of many disorders.[84]

The challenge with the increase of pathophysiologic knowledge will continue to be the lack of specific drugs for the treatment of gastrointestinal motor disorders. The pharmacotherapy currently available is very limited, and new medications are certainly needed. Hopefully, with continued basic science advances in the function of the enteric nervous system such as the identification of new receptors, new compounds will emerge, and the treatment and prognosis of children with primary motility disorders will improve.

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